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Part I Absorption and Metabolism . . .

A review of recent contributions

Part II Treatment of Iron Deficiency

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Iron . . .

Part I Absorption and Metabolism . . . A review of recent contributions

CALVIN W. WOODRUFF, M.D.*

Iron, although present in small amounts, plays widespread, continuous and fundamentally important roles in the body. It is part of hemoglobin (in red blood cells), myoglobin (in muscle cells), cytochromes and other enzyme systems necessary for the vital activities of cellular respiration and oxygen transport.

As our knowledge about the body's use of iron is expanding, Granick's[1] original hypothesis that iron is absorbed only to the extent it is needed by the body appears to be more relative than absolute. Disturbances of iron metabolism may lead to iron deficiency or iron excess in the body. Iron deficiency may lead to hypochromic, microcytic anemia, one of the most common anemias. Iron excess occurs in hemochromatosis, transfusion hemosiderosis and nutritional cytosiderosis, a disease found among the Bantus of Africa. Thus, the physiology of iron absorption continues to be a challenging problem.

METHODS OF MEASURING IRON ABSORPTION

Prior to 1930 methods of measuring iron absorption were imperfect. Since 1930 four methods of measuring iron absorption have been developed: (1) *chemical balance method* in which the difference between ingested iron and iron excreted is determined chemically; (2) *radio iron used in hemoglobin formation method* in which it is assumed that all ingested iron is utilized for hemoglobin formation; (3) *radioactive balance method* in which the difference between the radioactivity of tagged iron ingested and that excreted in the feces is determined, and (4) *postabsorptive or "tolerance" curves of serum iron method* in which the difference between rates of absorption and utilization is determined. However, in light of our present knowledge of iron metabolism, neither method two nor four is a good measure of true absorption.

In a recent critical review of iron absorption methods, Josephs[2] stated that none of these four methods is ideal. He feels, however, that balance studies should be the standard for judging other methods. Although both types of iron balance studies can be equally accurate, the chemical method offers a greater chance for inadvertent errors. The chemical method, however, has the advantage of permitting repeated periods of observation in a single subject. The radioactive balance method (although confined to one observation in each subject which may result in greater scatter and consequent uncertainty) has the advantage of greater ease of measurement with less chance for unaccounted traces of iron.

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FOOD IRON ABSORPTION STUDIES

Before isotopes were available for research it was a very tedious, painstaking task to determine absorption of iron from foods. So, prior to the use of isotopes, our knowledge about iron absorption was based upon the feeding of inorganic iron salts to test subjects. These studies showed that humans absorb iron most efficiently in its ferrous form.

Since the advent of isotopes our knowledge about food iron absorption has been expanding. Moore[3] was one of the first to study iron absorption using tagged foods. He used eggs and meat from chickens injected with Fe^{59}, milk and meat from cows injected with Fe^{59} and vegetables grown in nutrient solutions containing radioiron. The foods were cooked or prepared as they would be in a normal diet and then fed to fasting subjects. The normal adults, with very few exceptions, absorbed less than 10% of the food iron while iron-deficient adults absorbed slightly more. The addition of one gram of ascorbic acid, as crystalline ascorbic acid, increased the total iron absorption in every case, with the iron-deficient subjects showing slightly more absorption than the normal ones. The addition of ascorbic acid especially affected the absorption of egg iron by iron-deficient subjects, with the increased absorption ranging from under 10% to as high as 80 per cent. Similar, but less dramatic, responses followed the addition of large doses of ascorbic acid to radioiron-tagged liver and vegetables. Also, lower absorption of iron was noted when ferrous sulphate was fed with eggs than when fed alone on an empty stomach. The association of egg iron with phosphates[4] may account for its poor absorption.

Similar iron absorption studies with infants[5] indicate that about 10% of the iron in milk, cereal and egg is absorbed by infants and pre-school children. Insofar as milk is concerned, normal infants absorb 9.1% of the iron and iron-deficient infants absorb 16% of the iron as compared with 2.8% iron absorption by normal adult males. The mean figures of iron absorption by infants from regular-sized portions of cereals and eggs are 12.3% and 11.0%, respectively. Again, the iron-deficient subjects absorbed slightly more iron than those who were not anemic. However, in contrast to eggs, when ferrous sulphate is added to milk the iron is as efficiently absorbed by infants as is the iron in a similar dose of ferrous sulphate given alone on an empty stomach.

This information concerning the absorption of iron from food suggests figures for iron absorption from milk by infants which are considerably lower than those derived from balance studies.[2] In contrast with adults, infants seem to show reasonably good agreement between their iron absorption, as measured by difference between intake and stool excretion, and the amounts of iron found in their circulating hemoglobin. The relatively poor absorption of iron from spinach and some other vegetables noted in older chemical balance studies has been confirmed. It also appears that eggs are not so good a source of food iron as their relatively high iron content would suggest.

The iron absorption of premature and full-term new born infants also has been studied.[8] An uptake of 3% was found when using tracer doses without any

carrier iron. These results show that the mechanisms for absorbing iron are operative from birth, but at this early age cannot be translated into terms of absorption for food iron.

Studies indicate that infants and pre-school children probably absorb about 10% of the iron in their diets whereas normal adults probably absorb somewhat smaller amounts.

ABSORPTION OF MEDICINAL IRON

The absorption of medicinal iron also has been the subject of several recent studies.

Most of the past studies on medicinal iron retention have been made on adults. In normal cases retention has been found to be low, usually less than ten per cent. Most of these studies, conducted generally with ferrous salts, and with the dosages ranging from 0.5 - 1.0 mg/Kg/d, indicate the amount of iron absorption is 2 - 20% for normal individuals and 20 - 60% for hypochromic anemia subjects.

Still of keen interest, although conducted several years ago, is a study of pregnant women in which the per cent absorption of a dose of medicinal iron was related both to the size of the dose and to the time when administered during pregnancy.[6] It showed that iron absorption, and presumably iron need, increased during the latter half of normal pregnancy. This study demonstrated quite clearly that, at any specific week of gestation, increasing the dose of medicinal iron from 2 to 120 mg. resulted in a progressive diminution of the percentage of absorbed iron used for hemoglobin formation. The relationship between dose administered and per cent absorbed showed no observable *net* increase in uptake under 15 weeks gestation by increasing the dose from 40 to 120 mg. There was a slight increase in uptake over the dosage range in later pregnancy. The increase was less than 3 mg. when the dose was tripled. Consequently, all observations concerning the absorption of medicinal iron must take into account that the percentage absorbed (or the percentage utilized) will depend to a very large extent upon physiologic need as well as the size of dose administered. These observations have recently been confirmed in iron deficient infants.[7]

Several studies suggest that iron is best absorbed if given to patients when they are in a fasting state and that the amount of medicinal iron absorbed varies inversely with the bulk of the meal with which it is fed. Even the addition of orange juice (although it is high in ascorbic acid which aids in changing ferric iron to the more easily absorbed ferrous iron) to a dose of medicinal iron reduces the effective absorption of the iron. Consequently, therapeutic iron should be given on an empty stomach.

The studies of medicinal iron retention by children are less numerous than are those done with adults. In general, the studies show a relatively higher retention of iron in children than in adults, and that there is little difference in iron absorption in normal and anemic children.

Claims have been published that combined administration of copper and iron in the treatment of hypochromic anemia in adults is more effective than iron alone. The results of these earlier studies have not been confirmed by more recent critical studies. (Also, even a very poor American diet contains considerable copper. Since no copper deficiency in adults has been recognized, the value of adding copper to medicinal iron for adults seems of doubtful value.)

There may be some unusual cases of hypochromic anemia in infancy and early childhood in which therapeutic effectiveness of iron is achieved when copper is given with the iron. Moore[21] has noted a second reticulocyte response when copper was added to iron, after two weeks of therapy with ferrous sulphate alone, suggesting the presence of a copper deficiency as well. However, research and clinical findings indicate that, even among infants, copper deficiency must be exceedingly rare.

During the past decade, the therapeutic value of cobalt in the treatment of human anemias has been extensively explored. The claim that cobalt improves utilization of iron appears doubtful. If cobalt does exert a beneficial effect it probably is via its temporary polycythemia-producing effect (the ability to increase red blood cell formation). The cobalt is usually administered orally as cobaltus chloride, but parenteral therapy has also been used. Further research is needed before a final evaluation of this property of cobalt can be made.

ABNORMALITIES OF IRON ABSORPTION

Knowledge of what abnormalities may occur in the iron absorption process in the human body is especially important when determining the dose size and method of administering the medicinal iron.

The early theory that iron is absorbed by the body according to need led to the mucosal block concept. Thus, for awhile it was believed that the intestinal mucosa is able to accelerate or decrease iron absorption according to the amount of iron needed. Evidence that patients with hypochromic anemia (an iron deficiency state) absorb iron more efficiently than do normal persons gave support to this theory. Later, however, Dubach et al.[21] showed that patients with pernicious anemia also absorb iron well and so disproved the relation between need and absorption of iron. Another example of this breakdown of the mucosal block concept is the study of iron toxicity in rabbits and dogs by Reissman et al.[16] These researchers found that the administration of solutions of iron at high levels of about 22 mg/Kg was followed by very high rises in serum iron within one hour, the levels going as high as ten times those of total iron-binding protein in the blood. This occurred even though the actual amount of iron absorbed was a very low percentage of the iron in the intestines. Tests showed that the intestinal walls of the experimental animals were normal, both microscopically and functionally. Actually, in these experimental animals, rectal administration gave serum iron values that were just as high as those obtained with stomach or duodenal iron administration. There is every reason to believe that similar abnormal absorption mechanisms operate in infants with ferrous sulphate

poisoning. Thus, one must conclude that if the iron dose is high enough toxic amounts will be absorbed.

In hemochromatosis the body contains large amounts of iron in both of the chief storage organs, the liver and spleen, and the iron-binding protein in the plasma is saturated with iron. Yet it is possible to demonstrate that some of these patients do absorb iron at a rate greater than normal,[10] while others seem to have a normal rate of assimilation. So again the mucosal block concept does not apply to this disease.

Another contradiction of the theory that iron is absorbed by the body as needed is the case of a single patient with hypochromic anemia who failed to absorb oral iron.[11] This patient was able, however, to use in a relatively normal manner iron given intravenously. Even though this case represents a rare defect in iron absorption, it further emphasizes that not all the mechanisms for controlling iron absorption have been elucidated.

Mechanisms for controlling iron absorption seem to be more relative than absolute. Over the dosage range found with medicinal iron, the per cent absorption is inversely related to the dosage level. Local factors, such as the bulk of the meal ingested with the iron, the presence of large amounts of reducing agents, and the presence of phosphates may play a part in the efficiency of iron absorption. Specific defects which cause extremely low or abnormally high absorption also may occur.

FERROKINETICS

Ferrokinetics, the study of the dynamic metabolism of iron following intravenous injections of tracer doses, has been very useful in the study of many pathological states.

The technique used in ferrokinetics[12] is: (1) a solution of transferrin, the iron-binding protein found in blood plasma, is tagged with radioiron and is injected intravenously; (2) the rate at which the radioactivity disappears from the plasma is then determined, and (3) the rate of its appearance in the red cells is also measured. This new technique permits the study of the turnover time of plasma iron, the volume of the "labile pool" of iron, the rate of red cell formation and the life-span of red cells. As would be expected, the ferrokinetic patterns in diseases such as iron deficiency anemia, hemochromatosis, acute blood loss, hypoplastic anemia, hemolytic anemia and pernicious anemia are different from each other as well as different from the ferrokinetic pattern of normal persons.

Recent work on ferrokinetics shows that the iron in the plasma of a normal adult is low (about 125 mcg/100 ml or a total of 4 mg. per 70 K. adult), but the turnover rate is rapid (over 40 mg. of iron per day). Assuming daily minimal exchanges of one milligram each for storage, extra-cellular fluid and excretion, some 37 mg. a day go into the erythropoietic "labile pool." Of this 37 mg. of iron, normally 23 mg. a day are used in red cell synthesis and 14 mg. are returned to the plasma. Under normal circumstances an average adult male has

2,700 mg. of iron in circulating erythrocytes, 4 mg. in his plasma, 100 mg. in his labile pool, of which 30 mg. is undergoing hemoglobin synthesis in the bone marrow, and roughly 1,000 mg. in storage.

PREFERENTIAL DISPOSITION

One of the tenets of iron metabolism has been that enzyme iron is "inviolate," i.e., when an enzyme needs iron it has first call on any available iron. Recent studies of Buetler[13] show that there is a depressed cytochrome C (an iron-containing enzyme) activity in the livers of iron-deficient rats. This demonstrates quite clearly that certain iron-containing enzyme systems are unable to compete successfully with hemoglobin for available supplies of iron in the presence of an iron-deficiency. These findings fit in well with the clinical observations of iron-deficient patients who during treatment report an increased feeling of well-being before an increase in red cell count occurs. This suggests that in humans, too, there may be an early return to "normal" of some of the iron-containing enzymes before hemoglobin needs can be filled.

Beutler's studies also have created increased interest in what happens to the amount of dietary or medicinal iron absorbed and not used for hemoglobin synthesis. This portion of absorbed iron may prove to have much greater significance than was formerly supposed.

IRON EXCESSES

Recent studies suggest that the long-term ingestion of large amounts of iron are not innocuous. Certainly the incidence of cytosiderosis in the Bantu of South Africa who consumes a diet furnishing some 200 mg. of iron a day is pertinent to this question.[14] Although nutritional cytosiderosis, hemosiderosis and hemochromatosis are diseases characterized by large storages of iron in the body, their pathological patterns are quite different. Pathological studies show that the excess iron absorbed in cytosiderosis is largely deposited in the spleen. Cirrhosis of the liver is not common in patients with cytosiderosis. In hemochromatosis, the iron excess is frequently associated with cirrhosis of the liver, diabetes, and evidence of myocardial damage; the iron deposits are found almost exclusively in the liver. Findings to date indicate that the accompanying cirrhosis and diabetes of these diseases are not due to iron excesses alone. There is reason to believe that, although the excess iron may precipitate the cirrhosis and diabetes, there is some unknown factor that helps produce this disease. Hemosiderosis is the term used for the excess iron accumulation following repeated transfusions and repeated parenteral iron therapy.

Evidence has been gathered which indicates there is a close correlation between cytosiderosis and the serum iron levels of people within the same population group.[15] Ten individuals having little or no cytosiderosis had an average serum iron of 147 mcg. per cent while those having definite hemosiderosis had an average serum iron of 278 mcg. per cent. However, once a large amount

of iron was accumlated, there no longer was a direct correlation between the excess iron and the serum iron.

IRON TOXICITY

An interesting study concerning ferrous sulphate toxicity in dogs has demonstrated quite clearly that the symptoms of iron poisoning are associated with the amount of iron in the serum in excess of the iron bound to transferrin.[16] Within one or two hours after giving dogs 750 mg. of ferrous sulphate per Kg. of body weight, the serum iron was as high as 5,000 mcg. per cent and a very severe metabolic acidosis ensued. The acidosis, it was believed, was due to the formation of ferric hydroxide and the liberation of hydrogen ions in the circulating blood, causing a dramatic fall in the pH and bicarbonate concentration. The acidosis was accompanied by hypernea and evidence of a breakdown in normal glucose metabolism, accumulations of lactic and citric acids in the blood.

Despite clinical reports of over 40 cases of ferrous sulphate poisoning in children,[17] metabolic acidosis was found in the only case in which appropriate measurements were made. Apparently iron poisoning leads to increased capillary permeability and a 25% fall in plasma volume within four hours, causing increased cardiac output and sudden cardiovascular collapse. These symptoms are seen in infants who have ingested from 3 to 10 gm. of ferrous sulphate. The infants who survive the first six hours develop a state of seeming improvement which lasts for 10 to 14 hours; then sudden irreversible collapse may occur. Since the symptoms in infants have usually followed the oral ingestions of enteric coated pills, the local necrosis in the intestinal tract has been thought responsible for some of the toxic manifestations. Similar necrosis is conspicuously absent in animals given large doses of iron in solution. Thus, necrosis probably is not an essential part of the picture of iron poisoning. Certainly the clinical picture of ferrous sulphate poisoning must be largely attributed to (1) the absorption of iron in excess of the ability of the transferrin to maintain it in its innocuous, chelated form and (2) the toxic effects of ionized iron on tissues.

Treatment of iron toxicity should be directed toward removing any unabsorbed iron from the intestinal tract in any way possible, including possible surgical removal of undissolved tablets, and to giving support to the failing circulation. Since the ionized iron in the blood apparently is nondialyzable, exchange transfusion seems to be the only possible way to deal with the toxic iron. This procedure, however, may not be warranted since the absorbed iron rapidly disappears from the blood.

DAILY IRON NEEDS

In the past most of our knowledge concerning the requirements of adults for iron has been based on dietary studies, some estimates of absorption, and limited data concerning the loss of iron from the body in terms of urinary excretion, desquamation of cells etc.

In 1959 Finch[18] reported measuring the iron turnover and the biological half-life of iron in human adults who were in iron equilibrium, insofar as he could determine. He measured both the red cell iron and the component of tissue iron which was in equilibrium with the red cell iron. This component probably was less than the known stores of iron which are probably not in equilibrium with the plasma iron in normal individuals. Beginning one year after intravenous administration there was a steady, linear decrease in radioiron concentration. The turnover rate was calculated and expressed as the daily absorption or excretion of iron. For men, this was 0.61 $\pm$ 0.08 mg. per day. The red cell iron and miscible iron pools were smaller in non-menstruating females and the turnover was somewhat greater, giving an almost identical figure of 0.64 $\pm$ 0.05 mg. per day. In menstruating females the pool turnover was twice that of non-menstruating females and the daily iron turnover was 1.2 $\pm$ 0.11 mg. per day. These are by far the most nearly accurate figures concerning the daily iron turnover in humans that have ever been presented. This excellent experiment has confirmed much of our knowledge of iron needs previously based largely on calculations and extrapolations from known data.

Part II Treatment of Iron Deficiency

Iron deficiency of clinical importance results in the appearance of anemia since iron is an essential constituent of the hemoglobin of the blood. Normal concentrations of hemoglobin in the blood vary depending upon the age and sex of individuals. At birth hemoglobin concentration averages 17.0 gms. per 100 ml. and falls during the first 3 months of life to an average of 11.5 gms. per 100 ml. Normal concentrations rise gradually during childhood. At adolescence the normal value for males rises to 16.0 gms. per cent while females normally have a lower concentration of 14.0 gms. per cent. During the latter half of pregnancy there is a fall in hemoglobin concentration which is produced by the retention of fluids by the body and should not be interpreted as anemia.

The anemia of iron deficiency is morphologically a microcytic, hypochromic anemia. This means that the red blood cells are smaller than normal and less well filled with hemoglobin. The body appears to try to adapt to iron deficiency by making many small cells, apparently in an effort to use the available hemoglobin as efficiently as possible. There are a few other anemias, however, which are characterized by microcytic, hypochromic cells. They are Cooley's or Mediterranean anemia which is an inherited disorder, pyridoxine deficiency of which only a handful of cases have been reported in humans, and copper deficiency which has not been found to occur in man frequently enough for unqualified demonstration of a typical case (reported later).

Iron deficiency in infants and young children occurs because their dietary intake of iron is inadequate to meet the needs of growth. Prematures, twins, rapidly growing infants and those born after repeated pregnancies are particularly vulnerable to iron deficiency.[22] Most cases occur between the ages of 6 months and 2½ years but may be seen up to the age of 5 years. After this age iron deficiency anemia is practically never due to an inadequate intake, but, as in adults, it is due to blood loss.

It has been calculated that a normal adult who had no iron intake at all would not become deficient for over 5 years since the body-iron is reutilized and there is no mechanism for its excretion.[23] Consequently, iron deficiency anemia in an older child or adult is a signal that blood has been lost. This may occur intermittently in small amounts from an asymptomatic ulcer or an unsuspected tumor and may not be found on a single examination. In women of reproductive age it is most frequently due to excessive menstrual loss which has not been recognized. Actual scientific information on the amount of iron lost in the menses is somewhat limited in amount but large variations are known to occur in otherwise normal women.[24] Pregnancy apparently requires slightly more iron than the menstrual losses which cease during this period.

The recognition of iron deficiency in adults should lead to appropriate diagnostic tests at the same time that the iron deficiency is being treated. Occasionally the anemia is life-threatening in its severity and blood transfusions need to be given. In the vast majority of cases treatment with oral iron preparations is indicated and is almost invariably successful when carried out conscientiously unless bleeding continues.

Before discussing the various iron preparations which can be used it is necessary to consider dosage and duration of therapy. The dosage of iron can be discussed clearly only in terms of the amount of elemental iron in a preparation since iron salts differ in the amounts of iron which they contain. As noted in the section on iron absorption, large doses are less efficiently utilized than small ones. Thus there is little to be gained from excessive dosage except an increased frequency of undesirable side effects. The doses of iron usually recommended for treating adults are 200 to 400 mgm. per day in divided doses when the iron is in the form of inorganic ferrous salts. There is some recent evidence[25] that amounts of elemental iron as low as 100 mgm. daily are adequate for the treatment of even severe degrees of iron deficiency. Treatment of infants and children requires proportionately smaller doses. Usually 50 to 100 mgm. of elemental iron daily is sufficient. Larger doses, however, are frequently recommended since the regular administration of iron is not carried out by all patients. Adequate doses of iron will produce a rise in hemoglobin concentration of 0.1 to 0.2 gm./100 ml. of hemoglobin daily and the anemia should respond in 3 to 4 weeks.[26] Inasmuch as the body's iron stores are also depleted treatment should be continued for a month or two after the anemia has been corrected.

Since it has been known for many years that simple salts of inorganic iron are very effective in the treatment of iron deficiency, they should serve as our basis for comparison. Divalent ferrous salts are more readily absorbed by humans than the trivalent or ferric salts. It is probable that the latter are at least partially reduced in the normal intestine to ferrous salts because they have been used successfully for many years in the treatment of iron deficiency.

IRON PREPARATIONS

Ferrous sulfate is the commonly used iron preparation. It contains 36 per cent iron and the familiar 0.3 gm. enteric coated pill contains about 100 mg. of iron. The USP Elixir of Ferrous Sulfate, also in wide use, contains 32 mg. in 5 ml. Enteric coated ferrous sulfate tablets look like candy and their ingestion by children has resulted in a number of deaths.[17] They should always carry a "Keep out of reach of children" label.

Ferrous gluconate and other simple ferrous salts of organic radicals are less concentrated sources of iron and are said to produce fewer side effects, such as gastric irritation. When doses are determined on the basis of elemental iron they are the same as for ferrous sulfate. Ferric ammonium citrate and reduced iron are still in general use. They illustrate the fact that almost any inorganic iron preparation can be used to treat iron deficiency.

Various organic iron complexes have been introduced in the last few years and claims of reduced gastric irritation have been made. There is no evidence that they are more effective than ferrous sulfate. Chelated iron is the latest form studied. It has been shown to be less toxic than ferrous sulfate when given to dogs in large doses and to be effective in the treatment of iron deficiency.[27] Since critical studies have not been done, the lesser toxicity could be attributed to poorer absorption as well as to some unique property of the chelated form.

ACCESSORY FACTORS: Despite the clinical success of simple inorganic ferrous salts above, many combinations with other trace metals, vitamins, etc., have been suggested.

Copper: Copper is known to be essential for hemoglobin synthesis. Recently interest in the clinical role of copper in iron metabolism has increased because of the description of low serum copper levels in a syndrome of infancy associated with a defect in the metabolism of the serum proteins.[28, 29] The role of dietary copper deficiency in these cases has not yet been clearly defined. Suggestive evidence that copper deficiency may occasionally occur has been reported. At the present time there is no need to include copper therapy with iron preparations.

Cobalt: This important metal is an essential part of the vitamin B_{12} molecule and is used in that form by humans. Inorganic cobalt has a temporary stimulatory action upon red cell production which is probably mediated through erythropoietin, a recently discovered hormone-like substance which appears to be important in erythropoiesis. There is little evidence that the supplementation of iron therapy with cobalt has significant clinical benefit[29] and toxicity in small

infants has been described. The use of iron-cobalt mixtures does not appear warranted.

Molybdenum: Evidence that molybdenum increases the effectiveness of iron therapy is not sufficient to warrant recommendation for routine use.[29] In cattle, molybdenum in larger amounts in certain soils has been shown to precipitate copper deficiency.

Other factors: Liver preparations, ascorbic acid in 50 to 100 mg. doses and other substances have been incorporated in medicinal iron preparations. There is little evidence that such mixtures have therapeutic benefits in man greater than that of iron alone.

Parenteral iron therapy: Until recently several colloidal iron preparations for intravenous use were the only ones available. Their toxicity precluded their widespread use. The recent development of an intramuscular iron preparation[30] has put parenteral iron therapy in the hands of all medical practitioners. It is important that the dangers as well as the advantages of this iron-dextran complex be clearly understood. The body has no mechanisms for the excretion of an excess of iron and normally depends upon regulation of iron absorption to avoid excessive storage. Consequently, the relatively concentrated intramuscular preparation should only be used when iron deficiency has been definitely established. The dose must be carefully calculated from the severity of the anemia. Should anemia fail to respond to parenteral iron the diagnosis should be questioned before subsequent courses are given. Although intramuscular iron-dextran is much less toxic than previous intravenous preparations, animal experimentation and a few instances of untoward effects in man suggest that parenteral iron therapy should be reserved for those situations where oral therapy is not feasible.

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NUTRITIONAL PROBLEMS IN MEDICINE

Attention was focused on the importance of nutritional problems in medicine at a recent symposium sponsored by the Council on Foods and Nutrition of the American Medical Association and held in Nashville, Tennessee under the auspices of Vanderbilt University School of Medicine. The nutritional aspects of the cause and management of cardiovascular diseases and the dietary management of disorders of absorption from the intestine were discussed.

Nutritionists are principally interested in establishing the ideal diet for the cross section of a normal healthy population and nutritional biochemists attempt to unravel the intricate mechanisms involving the digestion, absorption and utilization of nutrients. Physicians on the other hand deal mostly with sick individuals in whom pathology is present. Stress often alters significantly the nutrient requirements, and greatly influences the kind and amount of various foods given the patient. The more the doctor is oriented toward the importance of these specialized nutritional aspects of the treatment of disease, the better will be the result in hastening the patient's recovery.

The use of low-sodium diets in conjunction with diuretic agents in the management of patients with congestive heart failure or hypertension requires a knowledge of special diet therapy that will achieve the desired result without distorting the nutritional balance. Unusual losses of potassium may become a problem in such patients and emphasizes the increasing role of mineral elements in medical practice.

That coronary artery disease can strike at an early age, was indicated by the report of evidence of coronary artery insufficiency in a number of young naval aviators, most of whom were overweight and who had elevated blood cholesterol levels and borderline hypertension.

Disease involving the gastrointestinal tract represents the largest percentage of most medical practices. For this reason, a review of the malabsorption syndrome and the importance of nutrition in this problem was most timely.

The malabsorption syndrome is probably more prevalent than ordinarily suspected. Excessive loss of fat in the stool, associated weight loss and frequent loose bowel movement should raise a high index of suspicion for the malabsorption syndrome.

As many as 40% of patients after surgery for ulcers develop absorptive difficulties of varying degree of severity. Vitamin and protein therapy are particularly important in the management of such patients. These individuals do not handle carbohydrate well and the excessive use of easily digested carbohydrate may lead to the so called "dumping syndrome." With large losses of fat seen in the malabsorption syndrome, the fat-soluble vitamins were particularly apt to be lacking.

Nutrition, one of the most continuing important factors in the life of individuals when in good health, becomes even more vital when sickness strikes. Doctors can better serve their patients by having a firm grasp of the fundamental nutritional principles embodied in the special problems involved in the diseased state. This symposium helped point the way for doctors to become more aware of the importance of nutrition in medicine. Much more follow-up is needed.

The Editor.